In the Claims:

What is claimed is:

1. (original) A pharmaceutical composition comprising an acetylcholinesterase inhibitor and an inverse agonist of the $GABA_A$ $\alpha1$ and/or $\alpha5$ receptor subtype wherein the inverse agonist has a functional efficacy at the $\alpha1$ and/or $\alpha5$ receptor subtypes of less than –5%, preferably less than –10%, and the efficacy measured at the $\alpha2$ and $\alpha3$ receptor subtypes is greater than 5% or preferably greater than 10%, and a pharmaceutically acceptable carrier, said composition being effective in the treatment of a cognitive disorder.

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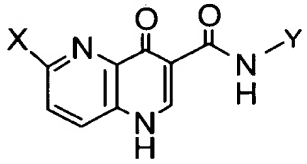
2. (original) The pharmaceutical composition of claim 1, wherein the inverse agonist has a functional potency (EC50 values) at the $\alpha1$ and/or $\alpha5$ receptor subtypes of 200 nM, preferably less than 150 nM.

3. (original) The pharmaceutical composition of claim 1, wherein the inverse agonist has a functional efficacy at the $\alpha5$ receptor subtype of less than –5%, preferably less than –10%, and the efficacy measured at the $\alpha1$, $\alpha2$ and $\alpha3$ receptor subtypes is greater than 5% or preferably greater than 10%.

4. (original) The pharmaceutical composition of claim 3, wherein the inverse agonist has a functional potency (EC50 values) at the $\alpha5$ receptor subtype of 200 nM, preferably less than 150 nM.

5. (original) The pharmaceutical composition of claim 1, wherein the inverse agonist at the $\alpha1$ and/or $\alpha5$ receptor subtypes has a binding Ki of 100 nM, preferably less than 30 nM.

6. (original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier, a $GABA_A$ inverse agonist, and an acetylcholinesterase inhibitor, wherein said $GABA_A$ inverse agonist is selected from a compound of Formula I below:



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wherein:

X is hydrogen, halogen, $-OR_1$, NR_2R_3, C_1-C_6 alkyl optionally substituted with up to three groups selected independently from halogen and hydroxy, or $-NR_2R_3$; or

X is phenyl, naphthyl, 1-(5,6,7,8-tetrahydro)naphthyl or 4-(1,2-dihydro)indenyl, pyridinyl, pyrimidyl, isoquinolinyl, 1,2,3,4-tetrahydroisoquinolinyl, benzofuranyl, benzothienyl, each of which is optionally substituted with up to three groups selected from halogen, C_1-C_6 alkyl, C_1-C_4 alkoxy, C_1-C_6 alkylthio, hydroxy, amino, mono or di(C_1-C_6) alkylamino, cyano, nitro, trifluoromethyl; or

X represents a carbocyclic group ("the X carbocyclic group") containing from
3 – 7 members, up to two of which members are optionally hetero atoms selected from oxygen and nitrogen, where the X carbocyclic group is optionally substituted with one or more groups selected from halogen, (C_1-C_6)alkoxy, mono- or di(C_1-C_6)alkylamino, sulfonamide, aza(C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkylthio, (C_1-C_6)alkylthio, phenylthio, or a heterocyclic group; and

Y is lower alkyl having 1 – 8 carbon atoms optionally substituted with up to two groups selected from halogen, (C_1-C_6)alkoxy, mono- or di(C_1-C_6)alkylamino, sulfonamide, aza(C_3-C_7)cycloalkyl, (C_3-C_7)cycloalkylthio, (C_1-C_6)alkylthio, phenylthio, a heterocyclic group, -OR_4, -NR_5R_6, SR_7, or aryl; or

Y is a carbocyclic group ("the Y carbocyclic group") having from 3 – 7 members atoms, where up to three of which members are optionally hetero atoms selected from oxygen and nitrogen and where any member of the Y carbocyclic group is optionally substituted with halogen, -OR_4, -NR_5R_6, SR_7, aryl or a heterocyclic group; and

R_1 is hydrogen, lower alkyl having 1 – 6 carbon atoms, or cycloalkyl having
3 –7 carbon atoms, where each alkyl may be optionally substituted with –OR_4 or –NR_5R_6;

R_2 and R_3 are the same or different and represent hydrogen, lower alkyl optionally mono- or disubstituted with alkyl, aryl, halogen, or mono- or di-lower alkyl;
aryl or aryl (C_1-C_6)alkyl where each aryl is optionally substituted with up to three groups selected from halogen, hydroxy, C_1-C_6 alkyl, C_1-C_6 alkoxy, or mono- or di (C_1-C_6)alkylamino;

cycloalkyl having 3 – 7 carbon atoms optionally mono or disubstituted with halogen, alkoxy , or mono- or di- lower alkyl; or

-SO_2R_8;

R_4 is as defined for R_1;

R_5 and R_6 carry the same definitions as R_2 and R_3, respectively;

R_7 is hydrogen, lower alkyl having 1 – 6 carbon atoms, or cycloalkyl having
3 – 7 atoms; and

R_8 is lower alkyl having 1 – 6 carbon atoms, cycloalkyl having 3 – 7 carbon atoms, or optionally substituted phenyl,

or a pharmaceutically acceptable prodrug thereof, or a pharmaceutically acceptable salt or solvate of said compound or prodrug,

said composition being effective in the treatment of a cognitive disorder.

7. (original) A pharmaceutical composition comprising a pharmaceutically acceptable carrier, a $GABA_A$ inverse agonist, and an acetylcholinesterase inhibitor, wherein the $GABA_A$ inverse agonist is selected from the group consisting of:

N-n-Butyl-6-chloro-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-n-Butyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,S-naphthyridine-3-carboxamide;

N-(2-Ethylthio)ethyl-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-n-Pentyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-Benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Tetrahydrofuranyl)methyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5 naphthyridine-3-carboxamide;

N-Isoamyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3 carboxamide;

N-(3-Methoxybenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Ethoxy)propyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-2-(2-Methyl)butyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3 carboxamide;

N-5-Pentanol-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-Benzyl-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Fluorobenzyl)-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Fluorobenzyl)-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Fluorobenzyl)-6-methoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4/5-Imidazolyl)methyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Thienyl)methyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Tetrahydropyranyl)methyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Fluorobenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3,5-Fluorobenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Fluorobenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Methoxybenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Methylbenzyl)-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-

carboxamide;

N-(2-Thienyl)methyl-6-(2-methoxyethoxy)-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Thienyl)methyl-6-morpholino-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(2-Thienyl)methyl-6-dimethylamino-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(4-Methylaminomethyl)benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide;

N-(3-Methylaminomethyl)benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5 naphthyridine-3-carboxamide hydrochloride;

N-[4-(Imidazolylmethy)lbenzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide,

a pharmaceutically acceptable prodrug thereof, and a pharmaceutically acceptable salt or solvate of said compound or prodrug,

said composition being effective in the treatment of a cognitive disorder.

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8. (original) The pharmaceutical composition of claim 7, wherein the $GABA_A$ inverse agonist is N-Benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide, or a prodrug thereof, or a pharmaceutically acceptable salt or solvate of said compound or prodrug.

9. (currently amended) The pharmaceutical composition of claim 7, wherein the acetylcholinesterase inhibitor is selected from the group consisting of ~~Aricept~~ (donepezil, ~~E2020~~), ~~Exelon~~ (rivastigmine), metrifonate, galantamine, physostigmine, tacrine, huperzine A, and icopezil, a prodrug thereof, and a pharmaceutically acceptable salt or solvate of said compound or prodrug.

10. (currently amended) The pharmaceutical composition of claim 9, wherein the acetylcholinesterase inhibitor is ~~Aricept (~~donepezil, ~~E2020~~) or a prodrug thereof, or a pharmaceutically acceptable salt or solvate of said compound or prodrug.

11. (currently amended) The pharmaceutical composition of claim 7, wherein the $GABA_A$ inverse agonist is N-Benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide, or a prodrug thereof, or a pharmaceutically acceptable salt or solvate of said compound or prodrug; and the acetylcholinesterase inhibitor is ~~Aricept (~~donepezil, ~~E2020~~) or a prodrug thereof, or a pharmaceutically acceptable salt or solvate of said compound or prodrug.

12. (original) A method for treating a cognitive disorder in a mammal, comprising administering to a mammal in need of such treatment an effective amount of a combination of a $GABA_A$ inverse agonist and an acetylcholinesterase inhibitor, wherein the $GABA_A$ inverse agonist and the acetylcholinesterase inhibitor are as defined in claim 1.

13. (original) The method of claim 12, wherein the $GABA_A$ inverse agonist is N-Benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide, or a prodrug thereof, or a pharmaceutically acceptable salt or solvate of said compound or prodrug.

14. (currently amended) The method of claim 12, wherein the acetylcholinesterase inhibitor is selected from the group consisting of ~~Aricept~~ (donepezil, ~~E2020~~), ~~Exelon~~ (rivastigmine), metrifonate, galantamine, physostigmine, tacrine, huperzine A, and icopezil, a prodrug thereof, and a pharmaceutically acceptable salt or solvate of said compound or prodrug.

15. (currently amended) The method of claim 12, wherein the acetylcholinesterase inhibitor is ~~Aricept~~ (donepezil, ~~E2020~~) or a prodrug thereof, or a pharmaceutically acceptable salt or solvate of said compound or prodrug.

16. (currently amended) The method of claim 12, wherein the $GABA_A$ inverse agonist is N-Benzyl-6-ethoxy-4-oxo-1,4-tetrahydro-1,5-naphthyridine-3-carboxamide, or a prodrug thereof, or a pharmaceutically acceptable salt or solvate of said compound or prodrug; and the acetylcholinesterase inhibitor is ~~Aricept~~ (donepezil, ~~E2020~~) or a prodrug thereof, or a pharmaceutically acceptable salt or solvate of said compound or prodrug.

17. (original) The method of claim 12, wherein the $GABA_A$ inverse agonist and the acetylcholinesterase inhibitor are administered separately.

18. (original) The method of claim 12, wherein the $GABA_A$ inverse agonist and the acetylcholinesterase inhibitor are administered sequentially.

19. (original) The method of claim 12, wherein the $GABA_A$ inverse agonist and the acetylcholinesterase inhibitor are administered simultaneously.

20. (original) The method of claim 12, wherein the cognitive disorder is selected from the group consisting of Alzheimer's disease, mild cognitive impairment, age-related cognitive decline, vascular dementia, Parkinson's disease, memory impairment associated with depression or anxiety, psychosis, Down's Syndrome, stroke, traumatic brain injury, and attention deficit disorder.

21. (original) The method of claim 20, wherein the cognitive disorder is Alzheimer's Disease.

22. (original) The method of claim 20, wherein the cognitive disorder is mild cognitive impairment.